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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/403,844	04/18/1995	OYSTEIN FODSTAD	7885.33USWO	4228

23552 7590 01/28/2003

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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	44

DATE MAILED: 01/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/403,844	FODSTAD ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *41,42,80-86,90,91,94,95,97,98,100 and 104* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-25,28,29,33-40,43,46,47,59,62,64,87-89,96,101,106,108-111,116 and 117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *See Continuation Sheet* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims pending in the application are 22-25,28,29,33-43,46,47,59,62,64,80-91,94-98,100,101,104,106,108-111,116 and 117.

Continuation of Disposition of Claims: Claims subject to restriction and/or election requirement are 22-25,28,29,33-43,46,47,59,62,64,80-91,94-98,100,101,104,106,108-111,116 and 117.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 11/7/02 in Paper No. 43 is acknowledged and has been entered. Claims 48, 51, 60, 61, 66, 67, 69, 71-75, 92, 93, 99, 102, 103, 105, and 112-115 have been cancelled. Claims 22, 39, 46, 59, 62, 64, 80, 83, 84, 87, 88, 89, 91, 96-98, 100, 101, 104, and 117 have been amended. Claims 41-42, 80-86, 90-91, 94, 95, 97, 98, 100, and 104 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Accordingly, claims 22-25, 28, 29, 33-43, 46-47, 59, 62, 64, 80-91, 94-98, 100-101, 104, 106, 108-111, and 116-117 are pending. Claims 22-25, 28, 29, 33-40, 43, 46-47, 59, 62, 64, 87-89, 96, 101, 106, 108-111, 116, and 117 are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 112/102/103

2. The rejection of claims 48, 51, 60, 61, 66, 67, 69, 71-75, 92, 93, 99, 102, 103, 105, and 112-115 are now moot in light of Applicant's cancellation of the claims.

Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 46-47, 106, and 117 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 46 is vague and indefinite because it is unclear what is encompassed in reciting the term "effective (for coating)". Specifically, it is unclear how the first antibody is "effective" for coating. Perhaps, Applicant intends that the first antibody coats a paramagnetic particle or bead without removing its antigen-binding ability.

Claim 117 is vague and indefinite because it is unclear what is encompassed in reciting the term "effective (for coating)". Specifically, it is unclear how the first antibody is "effective" for coating. Perhaps, Applicant intends that the first antibody coats a paramagnetic particle or bead without removing its antigen-binding ability.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 22-25, 28-29, 33, 36-38, 59, 62, 64, 101, and 108-111 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Widder et al. (EP 016,552) in view of Connelly et al. (US 5,422,277) and in further view of Abram et al. (US 4,497,900).

Widder et al. teach a method for separation of select population of cells from a mixed cell population using magnetic particles coated with a layer of specific antibodies which selectively bind to the select population. The coated microspheres with antibodies specific to target cells are contacted with the mixed population and the bound select population is magnetically separated from the mixed population (see page 4, last paragraph). The magnetically responsive microspheres have Protein A associated into the surface which selectively binds antibodies through the Fc region of the antibodies so that Fab arms of the antibodies extend outwardly for binding (see page 4, first paragraph). Widder et al. teach microspheres which are coupled with FITC conjugated rabbit IgG by incubation at 37°C for 20 minutes and examined (see page 10, Example 1). Furthermore, Widder et al. teach using the coated particles to separate red blood cells (RBC) from suspensions containing a mixture of different RBCs. Antibodies were coupled to the microspheres by incubation of 0.5 mg of the microspheres suspended in 0.2 ml. of 0.9% NaCl solution containing 0.1% Tween 80 (polyethylene sorbitans

monooleate). The RBCs were labeled with 51Cr and incubated with mild agitation and bound microspheres were separated and counted using a gamma counter (see page 11, Example 2).

Widder et al. differ from the instant invention in failing to teach incubation of the antibody coated microspheres in mild detergent for 5-10 minutes to 2 hours at 4°C.

Connelly et al. teach using Tween™ (polyethylene sorbitans monolaurate - Tween 20 or monooleate - Tween 80) as a detergent with fixatives so as not to destroy integrity and properties of the target cells. Connelly et al. specifically teach incubating the cells, therewith, for 20 minutes to 2 hours at temperatures ranging from 0°C to 37°C (see column 9, lines 20-48).

It would have been obvious to one of ordinary skill in the art to treat cells using the detergent taught by Connelly and incubate the cells at 0°C to 37°C in the method of Widder because mild detergents are well known and conventional in the art for removing extraneous matter from the cells without destroying integrity or other properties, i.e. viability, of the cells that may be necessary or required for subsequent use of the cells for assay or separation methods such as in the method of Widder.

Widder et al. and Connelly et al. fail to teach coating a first antibody to the paramagnetic particle wherein the first antibody is directed against a second antibody or antibody fragment that is directed against a cell membrane structure.

Abram et al. disclose an immunoassay for determining the presence of antigen wherein antigen-antibody complexes comprising antigen and antibodies (second antibody) are further incubated (treated) with a primary antibody (first

antibody=antiglobulin). Specifically, the primary antibody is directed against the secondary antibody that is bound to the antigen.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use antibodies directed to other antibodies such as taught by Abram to immobilize other antibodies on the surface of the magnetic particles such as in the method of Widder as modified by Connelly, because Abram specifically taught that a primary antibody directed against a secondary antibody can be used for binding two elements to form complexes, such as a label to an antigen (label -1° antibody- 2° antibody - analyte complexes) or a paramagnetic bead to a cell surface antigen (paramagnetic bead - 1° antibody - 2° antibody - cell surface antigen complexes) and Widder specifically has shown that immobilizing specific antibodies on a surface of a solid support, such as magnetic particles is conventional and well within ordinary skill.

In addition, given the combined teaching of Widder, Connelly, and Abram, the sensitivity levels recited in claims 62, 110, and 114 appear to be achieved by optimization procedures. It has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). Since Applicant has not disclosed that the specific limitations recited in instant claims 62, 110, and 114 are for any particular purpose or solve any stated problem and the combined teachings of the prior art appears to suggest the claimed

invention; absent evidence to the contrary, it would have been obvious for one of ordinary skill to discover the optimum workable value achieved by the methods disclosed in the prior art by normal optimization procedures.

5. Claims 46-47, and 106 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Widder et al. in view of Connelly et al. (US 5,422,277), in further view of Abram et al. (US 4,497,900), as applied to claims 22-25, 28-29, 33, 36-38, 59, 62, 64, 101, and 108-111 above, and further in view of Forrest et al. (U.S. Patent 4,659,678).

Widder et al., Connelly et al., and Abram et al. have been discussed supra. Widder et al. Connelly et al., and Abram et al. differ from the instant invention in failing to teach incorporating the antibodies, buffers, and reagent into a kit format.

Forrest et al teach a sandwich assay wherein a complex is formed between antigen in a sample and two or more antibody reagents and bound to solid supports such as magnetic or paramagnetic particles or beads having labeled or unlabeled antibodies attached thereto (see Abstract, column 1 and 2). The label employed may be selected from those known in the art such as fluorimetric or enzyme labeling. Forrest et al. teach using Protein A attached to the solid support and further attached to an antibody (see column 3-4). Forrest et al. teach using antibody reagents (which constitute intact antibodies or fragments thereof) that constitute a specific binding protein such as avidin and biotin and adding the reagents in any order so as to optimize the reaction conditions (column 5).

It would also have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the antibodies, buffers, beads, and reagent in the methods of Widder, Connelly, and Abram in a test kit arrangement such as taught by Forrest because test kits are conventional and well known in the art for their recognized advantages of convenience and economy.

6. Claims 34-35, 39-40, 43, 87-89, 96, and 116 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Widder et al. (EP 016,552) in view of Connelly et al. (US 5,422,277) and in further view of Abram et al. (US 4,497,900) as applied to claims 22-25, 28-29, 33, 36-38, 59, 62, 64, 101, and 108-111 above, and further in view of Kemmer et al. (Journal of Immunological Methods, 1992) or Holmes et al. (WO 91/09938).

Widder et al., Connelly et al., and Abram et al. have been discussed supra. Widder et al., Connelly et al., and Abram differ from the instant invention in failing to teach separation and detection of specific cells, in this case, cancer cells.

Kemmer et al. teach isolation of tumor cells from a mixed cell suspension of human tumor tissue which contains tumor cells, leucocytes, and erythrocytes, using magnetic beads coated with monoclonal antibodies.

Holmes et al. teach a method of separating hematopoietic progenitor cells from a mixed population of hematopoietic cells which contain malignant cells using microbeads coated with murine antibody which binds to the Fc portion of IgG murine antibodies or Protein A which reacts universally with the Fc portion of virtually all IgG antibodies (see

page 6, lines 8-24). The mixed population of Holmes et al. is commonly derived from the bone marrow mononuclear cells, fetal, and umbilical cord blood or adult human blood.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use the method of cell separation taught by Widder, as modified by Connelly and Abram, to separate cells from a variety of cell samples as taught by Kemmer and Holmes because Kemmer or Holmes teach that it is advantageous to remove tumor cells from a mixed population using magnetic microbeads coated with either monoclonal antibodies or protein A for the purpose of further studying the tumor cells or to purge a sample of tumor cells. The use of various monoclonal antibodies specific for antigens present on the cell surface for binding, separation, and detection is well known in the art and a skilled artisan would have had a reasonable expectation of success in choosing an antibody that is specific for an antigen present on the surface if the cell population of interest.

7. Claim 117 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Widder et al. in view of Connelly et al. (US 5,422,277), in further view of Abram et al. (US 4,497,900) as applied to claims 22-25, 28-29, 33, 36-38, 59, 62, 64, 101, and 108-111 above, and in further view of Kemmer et al. (Journal of Immunological Methods, 1992) and Forrest et al. (U.S. Patent 4,659,678).

Widder et al., Connelly et al., Abram et al., and Kemmer et al. have been discussed supra. Widder et al., Connelly et al., Abram et al., and Kemmer et al. differ

from the instant invention in failing to incorporate the antibodies, beads, buffers, and reagent into a kit format.

Forrest et al. has been discussed supra.

It would also have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the antibodies, buffers, beads, and reagent in the methods of Widder and modified by Connelly, Abram, Kemmer into a test kit arrangement such as taught by Forrest because test kits are conventional and well known in the art for their recognized advantages of convenience and economy.

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New Grounds of Rejection

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 22-25, 28-28, 33-40, 43, 59, 62, 64, 87-89, 96, 101, 108-111, 116, and 117 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide any literal support for the recitation of "detecting a specific living target cell in a cell suspension of mixed cell

population, or in a cell suspension prepared from a solid tissue, at a sensitivity of one target cell per 100 or more total cells".

The specification at pages 16-18 discloses a number of cell types and tissue samples from which cells are identified, targeted, and detected, i.e. micrometastatic neoplastic cells from blood and bone marrow, malignant cells from pleural or ascitic effusions, and subpopulations of normal cells, etc. but fails to provide literal support for the recitation of "detecting a specific living target cell in a cell suspension of mixed cell population, or in a cell suspension prepared from a solid tissue, at a sensitivity of one target cell per 100 or more total cells". Moreover, pages 18-23 of the specification exemplifies other cell types for use with the claimed invention but provides no literal or descriptive support for such recitation. Furthermore, none of the originally filed claims recited the limitation in question. Recitation of claim limitation lacking literal or descriptive support in the specification or originally filed claims constitutes new matter.

Response to Arguments

9. Applicant's arguments filed 11/7/02 have been fully considered but they are not persuasive.

A) Applicant argues that the combination of Widder, Connelly, and Abram does not render obvious the teaching of the claimed invention.

1) Applicant argues that Widder discloses coarse separation of cells through the use of microspheres having protein A, coated thereto.

In response to Applicant's argument that Widder uses protein A to coat the microspheres, independent claims 22, 46, and 87 recite "comprising" as open language; thus, claims 22, 46, and 87 do not exclude use of protein A as a coating for the claimed microspheres.

2) Applicant argues that Widder and Connelly fail to teach a first antibody that binds a second antibody.

In response to Applicant's argument that Widder and Connelly do not teach a first antibody that binds a second antibody, the rejection relies on the suggested use of a first antibody that binds a second antibody in the teaching of Abram, in combination with the teaching of Widder as modified by Connelly, for this obviousness rejection.

3) Applicant argues that Connelly fails to teach detecting a specific target cell at a sensitivity of one target cell per 100 or more total cells. Applicant contends that Connelly merely directs the reader to a cell fixative composition for fixing the internal components of a cell without disrupting the cell surface components.

In response, Connelly is relied upon for the teaching of Tween™ (polyethylene sorbitans monolaurate - Tween 20 or monooleate - Tween 80) used as a detergent with fixatives so as not to destroy integrity and properties of the target cells and of incubating the cells, therewith, for 20 minutes to 2 hours at temperatures ranging from 0°C to 37°C. Use of such mild detergent should provide inherent sensitivity of one target cell per 100 or more total cells because of the inherent property of the mild detergent to protect integrity and properties, i.e. sensitivity, of the target cells.

4) Applicant argues that the combination of Widder and Connelly is deficient since the combination results to a fixed population of cells that are no longer live as a result of use of fixative by Connelly.

In response, Connelly is relied upon in combination with Widder only for the teaching of use of a mild detergent Tween™ (polyethylene sorbitans monolaurate - Tween 20 or monooleate - Tween 80) so as not to destroy integrity and properties of the target cells and of incubating the cells, therewith, for 20 minutes to 2 hours at temperatures ranging from 0°C to 37°C. To reiterate, use of such mild detergent should provide inherent sensitivity of one target cell per 100 or more total cells because of the inherent property of the mild detergent to protect integrity and properties, i.e. sensitivity viability, of the target cells.

5) Applicant argues that Abram does not cure the deficiency of Widder and Connelly because the antibodies described by Abram are directed against antigens from cells, i.e. bacteria, that have been lysed. Further, Abrams does not teach coating the magnetic particles with a first antibody or antibody fragment directed against a second antibody for detecting target cells at the claimed concentration.

In response, the rejection is based on the combination of Widder in view of Connelly, and in further view of Abrams. Widder is relied upon for the coating of the paramagnetic particles with antibody. Connelly is relied upon only for the teaching of using mild detergent so as to preserve protection of integrity and other properties, i.e. sensitivity and viability, of the target cells. Additionally, Abrams is relied upon only for the teaching of antigen-antibody complex configuration comprising antigen and antibody

(second antibody) which is further linked with a primary antibody (first antibody=antiglobulin) wherein the primary antibody is directed against the secondary antibody that is bound to the antigen. Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to use antibodies directed to other antibodies such as taught by Abram to immobilize other antibodies on the surface of the magnetic particles such as in the method of Widder as modified by Connelly, because Abram specifically taught that a primary antibody directed against a secondary antibody can be used for binding two elements to form complexes, such as a label to an antigen (label -1° antibody- 2° antibody - analyte complexes) or a paramagnetic bead to a cell surface antigen (paramagnetic bead - 1° antibody - 2° antibody - cell surface antigen complexes) and Widder specifically has shown that immobilizing specific antibodies on a surface of a solid support, such as magnetic particles is conventional and well within ordinary skill.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

B) Applicant argues that the combination of Widder, Connelly, and Abrams with Forrest does not suggest the claimed invention because Forrest fails to overcome the deficiencies of Widder, Connelly, and Abrams.

The alleged deficiencies and responses thereto, regarding the combined teachings of Widder, Connelly, and Abrams is discussed supra. Forrest is combined with the teaching of Widder, Connelly, and Abrams only for the teaching of incorporating antibodies, paramagnetic particles, and reagents into a kit format. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the antibodies, paramagnetic particles, and reagents in the methods of Widder, Connelly, and Abrams in a test kit arrangement such as taught by Forrest because test kits are conventional and well known in the art for their recognized advantages of convenience and economy.

C) Applicant argues that the combination of Widder, Connelly, and Abrams with Kemmer et al. and Holmes et al. does not suggest the claimed invention because Kemmer et al. and Holmes et al. fail to overcome the deficiencies of Widder, Connelly, and Abrams.

The alleged deficiencies and responses thereto, regarding the combined teachings of Widder, Connelly, and Abrams is discussed supra. Kemmer is incorporated with the combined teaching of Widder, Connelly, and Abrams only for the teaching of isolating tumor cells from a mixed cell suspension, using magnetic beads coated with monoclonal antibodies. Alternatively, Holmes is incorporated with the combined teaching of Widder, Connelly, and Abrams only for the teaching of separating hematopoietic progenitor cells from a mixed population which contain malignant cells using microbeads coated with murine antibody which binds to the Fc portion of IgG

murine antibodies or Protein A which reacts universally with the Fc portion of virtually all IgG antibodies. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to use the method of cell separation taught by Widder, as modified by Connelly and Abram, to separate cancer cells from a heterogeneous cell mixture as taught by Kemmer or Holmes, because Kemmer or Holmes teaches that it is advantageous to enrich tumor cells from a mixed population using magnetic microbeads coated with either monoclonal antibodies or protein A for better isolation and identification of tumor cells, just as suggested by the combination of the methods of Widder, Connelly, and Abram.

D) Applicant argues that the combination of Widder, Connelly, and Abrams with Kemmer or Holmes and further with Forrest does not suggest the claimed invention because Forrest fails to overcome the deficiencies of Widder, Connelly, Abrams, and Kemmer or Holmes.

The alleged deficiencies and responses thereto, regarding the combined teachings of Widder, Connelly, Abrams, Kemmer, and Holmes is discussed supra. Forrest is combined with the teaching of Widder, Connelly, Abrams, Kemmer, and Holmes only for the teaching of incorporating antibodies, paramagnetic particles, and reagents into a kit format. It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the antibodies, paramagnetic particles, and reagents in the methods of Widder, Connelly, Abrams, Kemmer and Holmes in a

test kit arrangement such as taught by Forrest because test kits are conventional and well known in the art for their recognized advantages of convenience and economy.

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday to Thursday from 7:00

AM to 4:30 PM. The examiner can also be reached on alternate Fridays from 7:00 AM to 3:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (703) 308-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
Patent Examiner
Art Unit 1641

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

1/27/03